Dissecting the DNA and RNA Bound Proteome of Human Embryonic Stem Cells

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ABSTRACT

Background

Accumulating evidence supports the existence of dual-function DNA- and RNA- binding proteins (DRBPs) that coordinate multiple steps of gene expression programs, adding an additional level of complexity to gene regulation. Despite extensive research on DNA-binding proteins (DBPs) and RNA-binding proteins (RBPs), little is known about the identity and function of the dual binders.

Results

Using RNA-sequencing and mass-spectrometry, we generated a global map of gene expression profile in undifferentiated and differentiated cells and found that the vast majority of a literature-curated set of DRBPs are expressed in human embryonic stem cells (hESCs). Notably, DRBPs have higher mRNA and protein abundance compared with non-DNA and non-RNA binding genes and, surprisingly, also when contrasted with DBPs and RBPs. Differential expression analysis further shows that a large fraction of DRBPs are significantly up-regulated in hESCs, suggesting that DRBPs may shape the stem cell state. As a step towards the experimental identification of DRBPs, we performed RNA interactome [1-3] to capture the poly(A)-RNA bound proteome of hESCs. We show that the hESC interactome is enriched for known RBPs, including a substantial number of potential DRBPs.

Conclusions

Here we present the first, to our knowledge, RNA interactome of human ESCs. We further propose a novel solution to systematically uncover the in vivo repertoire of DNA- and RNA-binding proteins of hESCs. While identifying the full catalog of DRBPs is technically challenging, it has the potential to lead to the detection of key factors that have been overlooked when studying DNA and RNA regulation separately, hence contributing to both fields of gene regulation and stem cell biology.

References

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